Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

1-13. (Cancelled)

14. (Currently amended) A method of enhancing the cytotoxic sensitivity of neoplastic cells to an antifolate drug, said method comprising:

(a) delivering ~~into~~ directly to said neoplastic cells a vector, said vector comprising a DNA sequence encoding folylpolyglutamyl synthetase (FPGS), operably linked to a promoter, wherein said FPGS is expressed in said neoplastic cells at a level higher than the endogenous FPGS level of said neoplastic cells;

(b) treating the neoplastic cells in step (a) with an antifolate drug that is polyglutamated by said FPGS; and

(c) enhancing the cytotoxic sensitivity of said neoplastic cells to said antifolate drug.

15. (Previously presented) The method of claim 14, wherein said FPGS is a mammalian FPGS.

16. (Previously presented) The method of claim 15, wherein said mammalian FPGS is a human FPGS.

17. (Previously presented) The method of claim 15, wherein said antifolate drug is methotrexate, edatrexate, aminopterin, or a thymidylate synthetase inhibitor.

18. (Previously presented) The method of claim 17, wherein said antifolate drug is methotrexate or edatrexate.

19. (Previously presented) The method of claim 18, wherein said antifolate drug is edatrexate.

20. (Previously presented) The method of claim 16, wherein said antifolate drug is methotrexate.

21. (Previously presented) The method of claim 16, wherein said antifolate drug is edatrexate.

22. (Previously presented) The method of claim 14, wherein said vector is a viral vector.

23. (Previously presented) The method of claim 20, wherein said vector is a viral vector.

24. (Previously presented) The method of claim 21, wherein said vector is a viral vector.

25. (Previously presented) The method of claim 22, wherein said viral vector is derived from retrovirus, adenovirus, adeno-associated virus, herpes virus, poliovirus, papillomavirus, or lentivirus.

26. (Previously presented) The method of claim 25, wherein said viral vector is derived from retrovirus, adenovirus, or herpes virus.

27. (Previously presented) The method of claim 14, wherein said vector is non-viral.

28. (Currently amended) The method of claim 14, wherein said vector is ~~a~~ an attenuated prokaryotic vector, a cationic liposome, a fusogenic liposome, a DNA-adenovirus conjugate, a DNA-protein complex, a non-viral T7 autogene vector, a starburst polyamidoamine dendrimer, a cationic peptide, or a mammalian artificial chromosome.

29. (Currently amended) The method of claim 27, wherein said vector is ~~a~~ an attenuated prokaryotic vector.

30. (Currently amended) The method of claim 14, wherein said vector is delivered ~~into~~ directly to said neoplastic cells by direct injection of nucleic acid, particle-mediated gene transfer, or receptor-mediated gene transfer.

31. (Previously presented) The method of claim 14, wherein said neoplastic cells are breast cancer or colon cancer cells.

32. (Currently amended) A method of enhancing the cytotoxic sensitivity of neoplastic cells to methotrexate or edatrexate, said method comprising:

(a) delivering ~~into~~ directly to said neoplastic cells a vector, said vector comprising a DNA sequence encoding folylpolyglutamyl synthetase (FPGS), operably linked to a promoter, wherein said FPGS is expressed in said neoplastic cells at a level higher than the endogenous FPGS level of said neoplastic cells;

(b) treating the neoplastic cells of step (a) with methotrexate or edatrexate; and

(c) enhancing the cytotoxic sensitivity of said neoplastic cells to said methotrexate or edatrexate.

33. (Cancelled)

34. (Currently Amended) The method of claim ~~33~~ 14, wherein said vector is delivered directly ~~into~~ to said neoplastic cells by inoculation.

35. (Cancelled)

36. (Currently amended) The method of claim ~~35~~ 32, wherein said vector is delivered directly ~~into~~ to said neoplastic cells by inoculation.